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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,254	11/15/2001	John C. Reed	P-LJ 5037	8329

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EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/001,254	REED ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspond nce address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *1-13,19,22 and 24-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-18,20,21 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Re: Reed *et al.*

Date of Priority: November 17, 2000

Claims 1-52 are pending.

Claims 1-13, 19, 22, and 24-52 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 14-18, 20-21, and 23 are currently under prosecution.

The Election filed October 17, 2003 in response to the Office Action of September 17, 2003 is acknowledged and has been entered.

Applicant's election with traverse of Group 4, claims 14-21, and 23 (specific to DNA encoding SEQ ID NO:16) is acknowledged. The traversal is on the ground(s) that nucleic acid molecules encoding amino acid sequences SEQ ID NOs:6, 16 and 26 correspond to a form or domain of human IRAK-4 and that a search of prior art in relation to SEQ ID NO:16 will reveal art relevant to SEQ ID NOs:26 and 6. This argument has been considered and is found persuasive. Thus, in addition to nucleic acids encoding SEQ ID NO:16, the search and examination will be extended to include nucleic acid molecules encoding SEQ ID NOs:6 and 26. Applicants further argue that the claims of Group 1 should also be included with the search and examination of Group 4 because the claims of Group 4 are directed to nucleic acid molecules while the claims of Group 1 are directed to isolated polypeptides encoded by the

nucleic acid molecules of Group 4. Applicants argue that a thorough search of the recited nucleotide sequences will include a search of polypeptides encoded by the sequences. This is not found persuasive. MPEP 802.01 provides that restriction is proper between inventions that are independent or distinct. Here, the inventions of the various groups are distinct for the reasons set forth in the Action mailed September 17, 2003. Further, although the searches may reveal similar results, the burden of searching DNA and polypeptides is extremely high. Each sequence search includes a result set from approximately six different databases. Further, the examination of polypeptides may require different considerations than the examination of nucleic acid molecules. Thus, different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

A further note with regards to the election: Applicants have selected DNA encoding the amino acids of SEQ ID NOs:6, 16, and 26 which are all related to human IRAK4. The specification teaches (page 126) that SEQ ID NO:6 is an amino acid sequence for a human IRAK4 death domain (DD) and that SEQ ID NO:5 is a nucleotide sequence of a human IRAK4 DD. Thus, and in accordance with the restriction requirement, claims 20 and 21 will be searched/examined only to the extent that they read on an oligonucleotide or single strand DNA primer derived from SEQ ID NO:5 because all the other recited sequences are drawn to non-elected inventions.

Information Disclosure Statement

The Information Disclosure Statements filed on 03/03/2003, 09/30/2002, and 03/12/2002 have been considered. Copies of the signed 1449 forms are attached herein.

Specification

The specification is objected to for the following reason: The specification on page 1 does not include the provisional application number to which priority is claimed. Applicant should amend the specification to **60/367,360.**

The specification is further objected to with regards to the description of the following figures:

1) The description of Figure 3G (page 7) does not include a SEQ ID NO. for the nucleic acid sequence displayed in the Figure. In the absence of a sequence identifier for said sequence, Applicant must provide a computer readable form (CRF) copy of the sequence listing, an initial or substitute paper copy of the sequence listing, as well as any amendment directing its entry into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e-f) or 1.825(b) or 1.825(d). *Failure to supply the appropriate sequences identification numbers in response to this action will be considered non-responsive.*

2) The description (page 9) of Figures 10 and 11 does not make reference to Figures 10A and 10B or 11A, 11B, and 11C as so labeled in the Figures.

Claim Objections

Claims 14, 17-18, 20-21, and 23 are objected to as being drawn to and inclusive of non-elected subject matter. For example, Claims 14 and 17 should only be drawn to an isolated nucleic acid molecule encoding a polypeptide selected from the group consisting of: SEQ ID NOs: 6, 16, and 26 and DNA that hybridizes to the latter under moderately stringent conditions wherein said DNA encodes a biologically active death domain (DD). Applicants are requested to make the appropriate changes to reflect the elected subject matter.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 20-21, as written, do not sufficiently distinguish over nucleic acids as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-18, and 23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth an isolated nucleic acid molecule encoding a polypeptide selected from the group consisting of SEQ ID NOs:6, 16, and 26 and or the complete complements thereof and therefore the written description is not commensurate in scope with the claims inclusive of naturally occurring DNA that hybridizes under moderately stringent conditions to the latter nucleic acids wherein said DNA molecules have death domain (DD) functional activity.

With regards to the genes encoding the human form of IRAK4, the specification teaches (page 127) the full-length gene encoding the human form of the IRAK4 polypeptide of SEQ ID NO:16. The specification further teaches the death domain region of the human IRAK4 polypeptide corresponding to amino acids 9 to 106 (SEQ ID NO:6) of SEQ ID NO:16 (page 106). The specification further teaches a shorter form of the human IRAK4 gene that encodes the amino acids of SEQ ID NO:26.

However, the claims are broadly drawn to any and all naturally occurring DNA molecules that hybridize under moderately stringent conditions. This would include a substantial number of nucleic acids that do not possess the biological activity of a death domain such as nucleic acids that have as little at 60% sequence identity with the claimed sequences as the specification teaches that the phrase "moderately stringent hybridization" refers to conditions that permit target-DNA to bind a complementary nucleic acid that has about 60% identity to target-DNA. Furthermore, the conditions under which the stringent conditions are set forth are not

defined as the specification only sets forth preferable conditions equivalent to hybridization in 50% formamide, 5.times. Denhart's solution, 5.times. SSPE, 0.2% SDS at 42.degree. C., followed by washing in 0.2.times. SSPE, 0.2% SDS, at 42.degree. C. Furthermore, the functional activity ascribed to a DD in the claims is not specific. This could include any biological activity. Thus, the claims are drawn to a **genus** of polynucleotides.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. Some of these factors include disclosure of complete or partial structures, physical and/or chemical properties, functional characteristics, structure/function correlations, methods of making the claimed product(s), or any combination thereof. With regards to hybridizing nucleic acids; however, it is noted that the specification does not appear to specifically teach an example wherein the isolated nucleic acids encoding SEQ ID NOs:6, 16, or 26 were used under moderately stringent hybridization conditions for the isolation of nucleic acids that encode functional DD proteins. Further, the hybridization conditions as disclosed by the specification are not limiting and thus the claims read on the full range of conditions from low to highly stringent wherein the claimed hybridized polynucleotides read on polynucleotides that range from those that lack significant complementarity to those that are completely complementarity to the claimed complementary polynucleotide.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. Applicants should further refer to Example 9 of the revised interim Written Description Guidelines regarding hybridization language (see http://www.uspto.gov/web/menu/written.pdf).

Therefore, only an isolated nucleic acid molecule encoding a polypeptide selected from the group consisting of SEQ ID NOs:6, 16, and 26 and or the complete complements thereof, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 14-18, 20-21, 23 are rejected under 35 U.S.C. 102(a) as being anticipated by Watanabe *et al.* (GenEmbl/PRI Database, Accession No. AK000528, February 22, 2000).

Watanabe *et al.* teach an isolated nucleic acid molecule encoding a polypeptide that is 100% identical to SEQ ID NO:6 and 16. The nucleic acid molecule is 2820 basepairs long and does not consist of any one nucleic acid encoding SEQ ID NOs:14, 24, 28, 55, or 57. Watanabe *et al.* further teach recombinant expression of the death domain encoded polypeptide via culturing cells (signet-ring cells) comprising a vector (pME18SFL3) suitable for expression of the said death domain polypeptide. The polynucleotide of Watanabe *et al.* further encompasses an isolated nucleic acid molecule that is 100% identical to SEQ ID NO:5 which further reads on an oligonucleotide comprising between 15 and 300 contiguous nucleotides of SEQ ID NO:5 or a DNA primer comprising a nucleic acid sequence derived from SEQ ID NO:5. (see attached sequence comparisons).

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17, 20-21 are rejected under 35 U.S.C. 102(b) as being anticipated by EST Database, Accession No. AA114228, November 13, 1996, IDS.

Accession No. AA114228 discloses an isolated nucleic acid molecule encoding a polypeptide that is 100% identical to SEQ ID NO:26 that does not consist of a nucleic acid molecule encoding the amino acid sequence of any of SEQ ID Nos: 24 and 28 (see attached sequence comparison). The sequence further encompasses an oligonucleotide comprising between 15 and 300 contiguous nucleotides of SEQ ID NO:5 or a DNA primer comprising a nucleic acid sequence derived from SEQ ID NO:5.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 14-16, 18, 20-21, 23 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 6,440,663 (Scanlan *et al.*, October 1998).

US Patent No. 6440663 teaches an isolated nucleic acid molecule encoding a polypeptide that is 100% identical to SEQ ID NO:6 (see attached sequence comparision). The nucleic acid molecule is 833 basepairs long and does not consist of any one nucleic acid encoding SEQ ID NOs:14, 24, 28, 55, or 57. The patent further anticipates recombinant expression of the death domain encoded polypeptide via culturing cells comprising a vector suitable for expression of the polypeptide (abstract). The polynucleotide further encompasses an isolated nucleic acid molecule that is 100% identical to SEQ ID NO:5 which further reads on an oligonucleotide comprising between 15 and 300 contiguous nucleotides of SEQ ID NO:5 or a DNA primer comprising a nucleic acid sequence derived from SEQ ID NO:5. (see attached sequence comparisons).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at 571-272-0871. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
January 22, 2004